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Cost-effectiveness of non-invasive and non-pharmacological interventions for low back pain: a systematic literature review.

Lazaros Andronis¹, Philip Kinghorn¹, Suyin Qiao¹, David GT Whitehurst²⁻⁴, Susie Durrell⁵, Hugh McLeod¹

Authors' affiliations:

1. Health Economics Unit, Institute of Applied Health Research, University of Birmingham, Birmingham, UK
2. Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada
3. International Collaboration on Repair Discoveries (ICORD), Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada
4. Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Vancouver, British Columbia, Canada
5. Gloucestershire Hospitals NHS Foundation Trust, Gloucester, UK

Corresponding author:

Dr Lazaros Andronis, Health Economics Unit, University of Birmingham, Birmingham, UK Email: l.andronis@bham.ac.uk . Tel: +44 (0) 121 414 3197; Fax: +44 (0) 121 414 8969

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Abstract

Background

Low back pain (LBP) is a major health problem, having a substantial effect on peoples' quality of life and placing a significant economic burden on health care systems and, more broadly, societies. Many interventions to alleviate LBP are available but their cost-effectiveness is unclear.

Objectives

To identify, document and appraise studies reporting on the cost-effectiveness of non-invasive and non-pharmacological treatment options for LBP.

Methods

Relevant studies were identified through systematic searches in bibliographic databases (EMBASE, MEDLINE, PsycINFO, Cochrane Library, CINAHL and NHS Economic Evaluation Database), 'similar article' searches and reference list scanning. Study selection was carried out by three assessors, independently. Study quality was assessed using the Consensus on Health Economic Criteria checklist. Data were extracted using customized extraction forms.

Results

Thirty-three studies were identified. Study interventions were categorised as: (i) combined physical exercise and psychological therapy, (ii) physical exercise therapy only, (iii) information and education and, (iv) manual therapy . Interventions assessed within each category varied in terms of their components and delivery. In general, combined physical and psychological treatments, information and education interventions and manual therapies appeared to be cost-effective when compared with the study-specific comparators. There is inconsistent evidence around the cost-effectiveness of physical exercise programmes as a whole, with yoga, but not group exercise, being cost-effective.

Conclusions

The identified evidence suggests that combined physical and psychological treatments, medical yoga, information and education programmes, spinal manipulation and acupuncture are likely to be cost-effective options for LBP.

Key points for decision makers

- Differences across studies due to diversity in comparators and methods employed limit the comparability of studies and hinder drawing conclusions.
- Identified studies reported a variety of outcomes, most often incremental cost per quality-adjusted life year, but also additional cost per improvement in pain, quality of life or reduction in work absenteeism.
- Evidence suggests that combined physical and psychological treatments, medical yoga, information and education programmes, spinal manipulation and acupuncture are likely to be cost-effective options for LBP. Active exercise programmes are more equivocal in terms of cost-effectiveness.

1. Introduction

Low back pain (LBP) is one of the commonest health problems, with a lifetime prevalence of 80-85% [1]. In 2010, LBP ranked first in causes of global years lived with disability (defined as 'life lived in less than ideal health'), and third for global disability-adjusted life years (defined as 'the sum of years of life lost due to premature mortality and years lived with disability') for non-communicable diseases [2, 3].

The economic burden of LBP is equally substantial. Estimating this burden has been the focus of a number of studies over the past 15 years, most of which have a particular emphasis on North America and Europe [4-8]. A UK study published in 2000 (using 1998 prices) reported an upper estimate for the societal impact of LBP-related health service resource use and periods of work absence to be in excess of £12 billion. This estimate comprised £1.6 billion incurred through the provision of direct health care resources, £1.6 billion related to informal care and £9.1 billion associated with production losses (sometimes referred to as 'indirect' costs) due to morbidity. In the US, of the \$90.7 billion of total (i.e. both back pain related and unrelated) health care expenditures incurred by individuals with LBP in 1998, Luo and colleagues [6] estimated that \$26.3 billion were attributable to LBP. International evidence has provided some consistent findings; indirect costs represent the majority of overall costs, the provision of care by primary care practitioners and physiotherapists contributes 25-30% of direct healthcare costs, and chronic LBP patients account for a large proportion of total health care costs [4, 5, 8].

It is evident that significant savings—to both the health care system and society as a whole—are possible through improved management of LBP. However, there is a paucity of evidence on the cost-effectiveness of different LBP treatments. This is evident in the fact that primary care LBP researchers have explicitly identified the absence of such evidence, with consideration of 'cost-effectiveness' having recently been named as a leading research priority [9].

Many therapies are available for treatment of LBP [10]. Clinicians' recommendations for appropriate therapies can vary substantially, [11, 12] and there is considerable uncertainty regarding the respective value of such treatments and interventions [13]. The aim of this systematic review was to identify, document and appraise studies reporting on the cost-effectiveness of non-invasive and non-pharmacological interventions for LBP.

2. Methods

2.1 Study identification

We searched for economic evaluations of non-invasive and non-pharmacological interventions in six major electronic bibliographic databases (EMBASE, MEDLINE, PsycINFO, Cochrane Library, CINAHL and NHS Economic Evaluation Database). The review's protocol was not published. Searches covered the period from January 2000 to July 2015, and were informed by a list of safe and potentially beneficial non-invasive and non-pharmacological interventions included in guidelines published by the National Institute for Health and Care Excellence (NICE) in the UK [13] and the American Pain Society/American College of Physicians (APS/ACP) in the US [10]. These included various combined physical exercise and psychological treatments, physical exercise interventions, manual therapy programmes, and information and education programmes (see Online Resource 1). Acupuncture was included as a non-invasive intervention in line with the draft LBP guidance published by NICE in 2016 [14]. Employed search strategies comprised combinations of key words, synonyms, term variants, expressions and Medical Subject Heading (MeSH) terms. A sample search strategy can be found in the electronic supplementary material (Online Resource 1). Supplementary searches were carried out through a review of reference lists of key articles and previous systematic reviews known to the research team, through screening reference lists of articles included in the study and through carrying out 'similar article' searches in MEDLINE (via the PubMed interface).

2.2. Study selection

All identified articles were considered against a list of predetermined inclusion and exclusion criteria (Online Resource 1). Selection of articles was carried out by three reviewers (SQ, LA, and PK) independently. Disagreement in inclusion or exclusion was discussed between the reviewers. Selection was carried out in two stages. The first stage aimed to filter out clearly irrelevant publications and involved applying the inclusion criteria on each article's title and abstract. Publications which met the inclusion criteria at the first stage, as well as articles for which an exclusion or inclusion decision could not be made on the basis of their title and abstract alone, were forwarded to the second stage, where they were judged on the basis of their full text.

To identify and assess the available cost-effectiveness evidence, we targeted different types of economic evaluation studies. Economic evaluations are defined as comparative analyses of alternative technologies, interventions or programmes in terms of both their costs and consequences [15]. Three forms of economic evaluation are typically identified: cost-effectiveness analyses (CEA), cost-utility analyses (CUA), and cost-benefit analyses (CBA). In all three forms of

economic analysis, costs are measured in monetary terms. In CEA, consequences are captured as a simplistic, single, natural unit of outcome. In CUA, consequences are expressed in terms of quality adjusted life years (QALYs). QALYs are calculated by adjusting the time spent in a particular health state by the utility or disutility associated with that specific health state. One QALY is equivalent to one year of full health. Finally, in CBA the utility or disutility associated with a treatment or intervention is expressed as a monetary value.

2.3 Extraction, quality assessment and synthesis of relevant information

A customised data extraction form was created to record information on relevant aspects, such as bibliographic information (author(s), journal and year of publication), general information (country, population, interventions and comparators), methodological characteristics (type of economic evaluation, type of analysis, perspective, included costs and reported outcomes). Data were extracted by one reviewer (SQ) and were checked and verified by four of the reviewers (LA, DW, PK, and HM). Quality assessment of the identified studies was carried out by two reviewers (LA and SQ) using the Consensus on Health Economic Criteria (CHEC-list) checklist [16]. The CHEC-list was developed to provide a means of obtaining insights into the methodological quality of economic evaluation studies summarised in systematic reviews. The list has been used widely and is recommended in Cochrane reviews as a means of informing appraisal of the methodological quality of economic evaluations [17]. The list comprises 19 questions which were developed and agreed by 23 international experts over three rounds of a Delphi consensus building exercise. Each item of the CHEC-list was formulated as a question that can be answered by yes or no. The checklist does not make provisions for the calculation of numerical scores that summarise a study's quality, thus no such scores were calculated.

Negative answers to checklist items do not necessarily concede poor practice or result in bias. While no identified studies were discarded on the grounds of poor methodology, relevant limitations are explicitly discussed in the following section. Studies were grouped thematically, according to the type of the intervention they assess. Narrative synthesis was used to analyse, summarise and present the information provided in each of the selected articles.

3. Results

A total of 891 unique records identified through searches in bibliographic databases and other sources were considered for inclusion. Scanning these records on the basis of their title and abstract led to exclusion of 802 irrelevant records (stage 1). Full text assessment of the 89 potentially

relevant studies resulted in the exclusion of a further 56 records. The remaining 33 studies [18-50] comprised the final set of studies that formed the basis for this review. The PRISMA flowchart summarising the selection process is given in Figure 1.

3.1 Overview

All of the identified studies were carried out in developed countries and were published between 2002 and 2015. Of these studies, 26 were conducted in Europe (United Kingdom: 14, Norway: 3, Germany: 2, The Netherlands: 2, Finland: 2, Sweden: 1; Denmark: 1, Switzerland: 1), while the remaining seven studies were carried out in North America (United States: 4, Canada: 2) and Asia (South Korea: 1). Interventions assessed in the identified studies were categorised into the following groups: (i) combined physical exercise and psychological treatment (n=12), ii) physical exercise therapy (n=6), iii) manual therapy (n=10), and iv) information and education (n=5).

Characteristics of the identified studies, including the compared interventions, employed methodology and economic evaluation outcomes, are given in Table 2. Twenty-two studies undertook and reported CUA, in all of which outcomes were measured in terms of QALYs. Four studies were CEA [21, 24, 25, 29], typically looking into outcomes such as reduction in disability or pain. Two studies were CBA [19, 20], three reported both a CUA and a CEA [34, 37, 38] and two reported a CEA and a CBA [18, 46].

Indications on the methodological quality of the identified studies were obtained through assessment against the 19 items (questions) of the CHEC-list quality assessment checklist [16]. Answers to CHEC-list questions are presented in Table 1. Positive answers to these questions are considered to be indicative of good practice in undertaking and reporting economic evaluations. In all of the identified studies, the number of positive ('yes') answers exceeded those of negative or not applicable responses. Many of the negative responses were given to questions related to i) subjecting uncertain variables to sensitivity analysis, ii) discussing the generalisability of the obtained results, and iii) identifying and measuring all appropriate and relevant costs. While sensitivity analyses were present in the majority of the studies, these would often not target variables that the authors identify to be uncertain. An extensive discussion of findings' generalisability was often not present in cases where the authors conducted an evaluation of a particular, tailored programme provided by a specific payer. Last, questions related to identification and measurement of all appropriate and relevant costs received negative responses when costs relevant to the chosen perspective (e.g. productivity loss when a societal perspective was adopted) were not included.

In the majority of the studies, economic evaluation was carried out alongside clinical studies, most often randomised clinical trials (RCTs) (n=29). One study was based on both a randomised and a non-randomised trial [24] and two studies drew data from a prospective, sequential comparison of separate patient cohorts [47, 50]. Two studies synthesised information from different sources through decision analytic models [40, 49].

Typically, the time horizon for the analysis was 12 months and was dictated by the maximum follow up in clinical studies which provided data for the economic evaluations. Five studies reported results over a 6 month time horizon [23, 28, 30, 35, 50] and five studies looked at costs and benefits accruing between 12 and 24 months post intervention [19, 25, 26, 31, 38]. Only four studies reported results over time horizons longer than 24 months. Of these, two studies used data from clinical studies with long follow-up [18, 20] and two studies estimated cost-utility results by extrapolating over long time horizons using decision analytic models [40, 49]. In line with recommendations, discounting was carried out to account for the effect of preferential timing in six of the 10 [19, 20, 26, 31, 40, 49] studies which had a follow-up time greater than 12 months. Discounting was not explicitly mentioned in the remaining four studies [18, 21, 24, 33].

3.2 Findings of identified studies

Findings of each study, grouped according to the nature of the compared interventions, are given in the text below.

3.2.1 Combined physical exercise and psychological treatment interventions

Twelve studies looking into the cost-effectiveness of combined physical and psychological interventions were identified. Rogerson *et al.* [42] (USA, societal perspective) focused on a patient group with comparatively severe LPB symptoms, targeting patients screened to identify those at high risk of chronic disability with an intervention combining cognitive behavioural therapy (CBT) and physical therapy. From a societal perspective, the intervention dominated as a treatment strategy, with greater QALY gain and lower total costs. Similarly, Lamb *et al.* [41] (UK, health care system perspective) found that although the addition of CBT was associated with higher costs (compared to usual care and from a healthcare provider perspective), the favourable QALY gain associated with CBT resulted in a low incremental cost-effectiveness ratio (ICER) of £1,786 per QALY (valuation year: 2008) and a high probability of CBT being cost-effective.

Norton *et al.* [49] (USA, commercial payer perspective) constructed a decision analytic model to explore the short and long term cost and QALYs of CBT. Key inputs in this analysis, including the

likelihood of improvement and quality of life (QoL) values, were obtained from the RCT reported in Lamb *et al.* [41], as well as from the existing literature. Using a US healthcare payer perspective, Norton *et al.* [49] estimated the ICER for CBT versus usual care to be \$7,197 per QALY in the first year, and \$5,855 per QALY over a 10 year time horizon (valuation year 2008).

Four studies evaluated the use of the Keele risk stratification tool, a prognostic screening method which was developed to categorise patients by LBP prognosis to different targeted physiotherapy treatment regimes. The initial StarT Back RCT aimed to assess the effectiveness and cost-effectiveness of the tool [43, 45] (UK, health care system and societal perspectives). This was followed by the IMPaCT Back Study, which sought to determine the effect of implementing the tool on physicians' choices and patient outcomes [47, 50] (UK, health care system and societal perspectives). In addition to evidence on health outcomes, these studies offered patient level data on use of NHS health care resources, private patient payment and productivity losses. The initial study [43, 45] found the intervention to be cost-effective compared to current practice across all three risk defined sub-groups, with results ranging from dominance for the medium-risk group to a low ICER of £463 per QALY (valuation year: 2008) for the high-risk group [45]. The implementation study [47, 50] found the Keele stratification tool was cost-effective (resulting in cost savings and QALY gains of £124 and 0.023, respectively) only for the high-risk patients [50] (valuation year: 2008).

Four of the studies of CBT or interventions containing some psychosocial element report results which are ambiguous or open to debate. Whitehurst *et al.* [34] (UK, health care perspective) report a slightly greater clinical benefit from physical therapy than from a brief pain management programme (BPM) targeting psychosocial factors, but lower mean healthcare costs for the latter. In this study, the most cost-effective option is physical therapy (with a cost per QALY of £2,362 (valuation year: 2001)), though the authors suggest that BPM may be acceptable as an additional treatment option, if provided in fewer sessions [34].

Schweikert *et al.* [28] (Germany, societal perspective) set out to assess the cost-effectiveness of providing CBT in addition to usual care in patients with chronic LBP in Germany. This study, which had a follow-up period of just six months, showed no statistically significant difference in treatment costs between CBT and standard therapy, and no significant differences in health outcomes, expressed in QALYs. However, due to differences in indirect costs described as being of borderline significance, the authors indicated that the intervention would be cost saving from a societal perspective.

Similarly, Johnson *et al.* [33] (UK, health care system perspective) conducted a trial-based economic evaluation to determine the impact of a CBT-based exercise and education programme on resource use, costs and patient outcomes. While the intervention led to a small, non-significant reduction in pain and disability, use of resources and costs were low, resulting in an ICER of £5000 per additional QALY (valuation year: 2003). However, the authors suggest that changes detected in QALYs may have been due to bias associated with those patients who had consciously opted into CBT.

Skouen *et al.* [19] (Norway, societal perspective) carried out a CBA where the benefits of treatment were expressed in terms of productivity gains. The authors found that a light multidisciplinary treatment programme resulted in net benefit for men, but that there was no significant treatment effect for women. No significant differences in costs and benefits were found for a more substantial and extensive multidisciplinary treatment programme.

In the last study in this group, Critchley *et al.* [31] (UK, health care system perspective) sought to compare the effectiveness and cost-effectiveness of different types of physiotherapy for patients with chronic LBP. Three interventions were compared against each other: usual outpatient physiotherapy, spinal stabilisation classes and physiotherapist-led pain management classes which were informed by a cognitive-behavioural approach. The authors found all three physiotherapy programmes to result in reduced disability (measured by the Roland Disability Questionnaire), improved health-related QoL (measured by EQ-5D), and fewer days off work. In relation to cost-effectiveness, physiotherapist-led pain management appeared to be less costly and marginally more effective than the other interventions.

3.2.2 Physical exercise therapy interventions

Six studies assessed the health and economic benefits of exercise and physical activity programmes. All these studies conducted and reported CUAs, with Smeets *et al.* [38] also reporting a CEA (cost per reduction in disability).

Two studies assessed the costs and benefits of yoga, both of which were carried out on the basis of data collected from randomised controlled trials. In the first of them, Aboagye *et al.* [48] (Sweden, employer and societal perspectives) found yoga to be cost-effective from the employer's perspective compared to exercise therapy and self-care advice. From the employer's perspective, the authors estimated the ICER for yoga to be as low as EUR 4,984 per QALY (valuation year: 2011) when compared to self-care advice, and found that yoga is less costly and of equivalent effectiveness when compared to exercise. When considering productivity costs as part of a societal perspective,

Aboagye *et al.* [48] found that yoga would be a cost-effective option if decision makers deem that a QALY is worth EUR 11,500.

In the second study, Chuang *et al.* [44] (UK, health care system and societal perspectives) compared yoga in addition to usual care against usual care alone. From the health care perspective, the authors found yoga to be cost effective if decision makers were willing to pay up to £20,000 for an additional QALY (ICER of £13,606 per QALY, valuation year: 2008), while from a societal perspective yoga is associated with cost savings and a greater number of QALYs. Both studies were conducted in Europe (Sweden and the UK respectively), and as with the exercise studies, both adopted a 12 month follow-up.

Two studies looked at the cost-effectiveness of group exercise therapy. Henchoz *et al.* [39] (Switzerland, societal perspective) compared a 12 week long exercise programme supervised by a sports therapist against usual care comprising advice to exercise regularly, both of which were offered as a follow-up to an outpatient multidisciplinary rehabilitation programme. While the exercise programme resulted in improved disability and trunk muscle endurance, these improvements did not lead to economic benefits. The authors estimated that the addition of exercise as a follow up to a multidisciplinary programme resulted in an ICER of EUR 79,270 (valuation year: 2005) and concluded that group exercise is not cost-effective given commonly cited values of decision makers' willingness-to-pay (WTP) for a QALY. In a study comparing intensive group training against usual physiotherapy care, van der Roer *et al.* [37] (Netherlands, societal perspective) found that group exercise resulted in higher costs and no significant differences in QALYs as compared to standard physiotherapy. A main driver of the higher cost was the increased use of secondary and alternative care services in the exercise group.

Smeets *et al.* [38] (Netherlands, societal perspective) assessed the cost per one-point improvement in disability and cost per QALY for the comparison between: (i) 10 weeks of physical training (including aerobic training and muscle strengthening), (ii) 10 weeks of gradual assumption of patient relevant activities and problem solving training, and (iii) a combination of the two programmes. Findings suggested that whilst combined treatment was not cost-effective, graded activity plus problem solving training delivered as a single intervention was marginally more effective (in terms of QALYs and reduction in disability) than the active physical treatment programme and the combination programme, as it was associated with lower direct and indirect costs.

Rivero-Arias *et al.* [27] (UK, health care and societal perspectives) sought to evaluate the potential costs and benefits of physiotherapy treatment compared to usual advice given by a physiotherapist

for patients with subacute and chronic LBP. The analysis, which makes use of data from a randomised controlled trial, reported no significant differences QoL between the physiotherapy and advice groups, though they found physiotherapy treatment to be associated with significantly higher out-of-pocket expenditures for patients. Despite the relatively low ICER of physiotherapy treatment of £3,890 per QALY (valuation year: 2004), the higher out-of-pocket expenditures were a main influence in the authors' conclusion that physiotherapist advice should be the treatment of choice in patients with the particular level of LBP severity.

3.2.3 Information and education interventions

Five studies looked at the costs and benefits of interventions involving education and provision of information. Loisel *et al.* [18] (Canada, insurance provider perspective) compared clinical rehabilitation, an occupational intervention comprising visits to an occupational therapist and participatory work with ergonomists, and a combination of the above (Sherbrooke model) against standard care. Two analyses were undertaken: a CEA and a CBA. For the former, the authors compared the additional costs per number of days on full benefits (full compensation) due of absence from work, and found that the greatest savings were associated with the occupational intervention. For their CBA analysis, Loisel *et al.* [18] subtracted the additional gains from avoided work absence between each intervention and standard care, from the additional cost of the intervention as compared to standard care. The authors found that the Sherbrook model results in mean savings of \$18,585 per worker over 6.4 years (valuation year: 1998), although they acknowledge that there were no statistically significant differences in absenteeism avoided between the four interventions.

A similar outcome—the net monetary value due to avoided absenteeism—was explored in the study by Molde Hagen *et al.* [20] (Norway, societal perspective). This study compared a spine clinic examination and provision of advice and information against usual treatment in primary care. The authors used a CBA framework to explore the long term economic returns of the intervention, in terms of productivity gains due to reduced absenteeism. Findings suggest that spinal clinic care and advice led to significantly fewer days of sick leave at 1 and 3 year follow-up points, which translated to economic returns of approximately \$3,500 per person (valuation year: 1995) (though a net benefit value of \$2,822 per person is given in the abstract).

Strong and colleagues [29] (USA, insurer perspective) set out to evaluate the effectiveness and cost-effectiveness of psychologist-led and lay person-led back pain educational sessions. Information on resource use and effectiveness was obtained from two cohorts of primary care patients participating

in two RCTs. Costs included in the study related to expenditures for delivering the interventions and resource use within primary care. Effectiveness was measured in terms of the number of low impact days, i.e. days during which patients were satisfied with the level of back pain they experienced. Both the psychologist and lay person led interventions resulted in additional low-impact days. The additional cost per low-impact day was found to be \$9.70 and \$6.13 (valuation year not stated) for the lay and psychologist-led interventions.

In a more recent study, Jensen *et al.* [46] (Denmark, health care system, taxpayer and societal perspectives) looked at the cost-effectiveness of interventions aimed to enabling LBP patients who have been on sick leave to return to work. The authors compared a brief intervention comprising initial clinical examination followed by advice to increase physical activity against a multidisciplinary intervention, which, in addition to these components, included a tailored plan to facilitate return to work, co-ordinated by a case manager. Two analyses were conducted: a CEA from the perspective of the health care system in Denmark to determine the additional cost per a one-week reduction in sick leave, and a CBA, which adopted a societal perspective and included costs borne by the health care system and productivity losses. The authors [46] reported that the multidisciplinary intervention was more costly than the brief intervention, and, in general, did not result in fewer days of sick leave.

On the premise that psychosocial factors may play a part in preventing LBP from becoming chronic, Jellema *et al.* [32] (Netherlands, societal perspective) assessed the costs and effectiveness of a minimal intervention strategy aimed at psychosocial factors compared to usual care in patients with sub-acute LBP. The authors found no statistically significant differences in either costs or QALYs in their analysis based on complete trial data, which gave a relatively high ICER of EUR 47,348 (valuation year: 2002) for the minimal intervention strategy. These findings prompted the authors to suggest that usual care should not be replaced by the minimal intervention.

3.2.4 Manual therapy

Ten studies evaluating some form of manual therapy were identified. Four of these studies were CUA and were conducted in the UK [22, 23, 36]. The study by Williams *et al.* [23] (UK, health care system) investigated the cost-utility of osteopathy clinic services within general practices in the UK, as compared to standard care. The authors found the osteopathy clinic intervention to result in higher health care system costs for an increase in health functioning, and estimated an ICER for osteopathy of £3,560 per QALY (valuation year: 1999). However, the authors caution that the conclusion “was subject to considerable random error” and highlight a need for further research to substantiate these results and assess the generalisability of the approach.

The UK BEAM Trial Team [22] (UK, health care system and patient perspective) compared a 12 week exercise programme and a spinal manipulation package, along with combined treatment, to a comparator of best care. Findings of the study suggested that the cost-effectiveness of each programme would depend on decision makers' WTP for a QALY: if this value is much less than £3,800 (valuation year: 2000), 'best care' is likely to be the best strategy. If WTP lies between £3,800 and £8,700, the optimal treatment would be spinal manipulation followed by exercise (i.e. the 'combined' treatment). For WTP values well above £8,700, manipulation alone would be the most cost-effective treatment.

Hollinghurst *et al.* [36] (UK, health care system, patient and societal perspectives) consider three single interventions (massage, Alexander technique and exercise), as well as five iterations of combined treatments, with normal care as the comparator. In terms of the single intervention, exercise performed best in terms of incremental cost-effectiveness (£2,847 per QALY, valuation year: 2005). However, this was due to its low cost and it is noted that exercise performs badly in terms of pain free days. Among two-stage therapies, exercise combined with the Alexander technique was the optimal strategy (£5,332 per QALY).

Haas *et al.* [24] (USA, perspective not explicitly stated) calculated the total healthcare costs in relation to Medicare expenditure for chiropractic care and found that this option was associated with only moderately higher total costs than usual care, mainly due to fewer onward/external referrals. The cost per reduction in pain and disability score for chiropractic care was lower for chronic than for acute patients. The intervention becomes more cost effective for chronic patients at 12 months than at three months, though the opposite results are observed for acute patients.

Niemisto *et al.* [21, 25] (Finland, societal perspective) conducted a randomised controlled trial to compare physician consultation care combined with manipulative treatment and stabilising exercise against physician consultation. Findings were reported in two studies. The earlier of them [21] was based on 12 month follow up data and had a focus on the effectiveness of the treatments. The authors found no statistically significant differences in costs or health outcomes between the interventions, and calculated an additional cost of \$23 per one-point change in a pain visual analogue scale associated with the combined intervention (valuation year: 2002). In the more recent study [25], the finding that a combination of manipulative treatment with exercises and physician consultation is cost-effective appears to reverse. Although there were still statistically significant differences in QoL between the combined intervention and physician consultation, these were deemed to be clinically minor and total annual cost savings were higher in the control.

Four studies investigated the effectiveness of acupuncture, three of which were cost-utility analyses measuring QALYs derived from the SF-6D tariff set. Ratcliffe *et al.* [26] (UK, health care system perspective) used data from a RCT to estimate the cost and QALYs associated with a programme of individualised acupuncture treatments delivered by acupuncturists trained in traditional Chinese medicine. The intervention was compared with usual care in the UK. The analysis showed acupuncture to be associated with increased costs (largely due to the initial cost of delivering acupuncture treatment), improved QoL and QALYs (mean incremental gain of 0.027 QALYs over 2 years), and an ICER of £4241 per additional QALY gained (valuation year: 2002). Given the low additional cost for a modest improvement in QALYs, Ratcliffe and colleagues [26] suggest that, in the longer term, acupuncture care appears to be a cost-effective treatment for LBP.

The most complex intervention involving acupuncture was evaluated by Herman *et al.* [35] (Canada, employer, participant and societal perspectives), who label as 'naturopathic care' a combination of acupuncture, exercise, dietary advice, relaxation training and education. Cost-effectiveness was calculated from three perspectives: societal, employer and participant. Findings suggested that naturopathic care was cost effective from all perspectives and was dominant from the societal perspective, compared to standardized physiotherapy education.

In a study carried out in Germany, Witt *et al.* [30] (societal perspective) compared the provision of immediate acupuncture against delayed acupuncture, provided three months later. Two analyses were undertaken, the first on the basis of patients randomised to immediate or delayed acupuncture, and the second on the basis of patients who declined to be randomised and received immediate acupuncture. Data collected over a relatively short period of time (six months) showed immediate acupuncture to be cost-effective from a health service and societal perspective respectively.

Kim *et al.* [40] (South Korea, societal perspective) sought to assess the cost-effectiveness of acupuncture as a complement to routine care in the treatment of chronic LBP in South Korea. To this end, the authors [40] developed a decision analytic model and populated it with cost and effectiveness information from the literature. Kim and colleagues [40] found acupuncture to result in improved QoL compared to usual care, for a modest increase in costs, a finding similar to Ratcliffe *et al.* [26]. The ICER for this comparison was calculated to be \$2,759 per QALY gained (valuation year: 2009).

4. Discussion

This review identified 33 studies seeking to assess the costs and benefits of a wide range of non-invasive and non-pharmacological interventions for LBP. Studies were grouped into four categories, according to the type of intervention they evaluated. The diversity of the interventions and the setting in which the assessment took place, and the often marked differences in the inputs and evaluation methods employed makes comparisons between studies, even within the same category, difficult. Nevertheless, the review offers insights into the cost-effectiveness of a wealth of interventions.

4.1 Summary of findings

Combined physical exercise and psychological treatments comprised the largest and the most diverse group of interventions. The group included studies which evaluated the use of the Keele risk stratification tool to target physiotherapy treatments [43, 45, 47, 50], as well as studies on group exercise and education sessions [33], pain-management programmes [31, 34], stabilisation physiotherapy [31]), multidisciplinary programmes with input from different health care professionals [19, 41, 42, 49] as well as a psychologist-led intervention [28]. With one exception [34], the interventions were compared to usual care and were found to be cost-effective [28, 31, 33, 41-43, 45, 49]. In general, interventions were characterised by non-significant improvements in QALYs and modest increases in costs compared to comparators [31, 33, 34, 42, 43, 45, 47, 50], or the significance of these differences is not reported [41, 49].

Findings of studies evaluating physical exercise therapy interventions are inconclusive, which may be partially explained by differences in the assessed programmes and employed methods. Studies assessing medical yoga showed this type of activity to be cost-effective from a payer's perspective and suggest that it may result in averted loss of productivity [44, 48]. On the other hand, studies looking into structured exercise programmes are more cautious: although such programmes appeared to lead to small improvements in QoL, authors do not recommend their widespread use [27, 37-39]. In comparison to combined psychological and physical exercise interventions, physical exercise only interventions appear to be less cost-effective, but it would be interesting to see how the use of yoga, such as that described in the study by Chuang *et al.* [44], would compare to the interventions reported by Lamb *et al.* [41] and Foster *et al.* [47].

Studies evaluating interventions comprising provision of information and education are an equally diverse group. Interventions under assessment are usually multidisciplinary and comprise of clinical examination followed by information and advice. Three out of the five studies in this group employ CBA to estimate the benefit due to days on sick absence averted, net of the cost of the interventions

[18, 20, 46]. In general, interventions which have an ‘advice and information’ component appear to lead to reductions in absenteeism, which compensate for the modest increases in costs.

Studies assessing the costs and benefits of manual therapy typically compare spinal manipulation alone or in combination with other components—most often exercise—against usual care, or acupuncture. Bar the studies by Niemisto and colleagues [21, 25], the non-acupuncture studies in this category suggest that manual therapy is a cost-effective alternative to usual care. Interestingly, Niemisto *et al.* [21] found that manipulative treatment is cost-effective as compared to usual care at 12 months post intervention, but usual care becomes more cost-effective at the 2 year follow-up.

On the whole, the identified evidence on acupuncture interventions is supportive of the idea that provision of acupuncture—either on its own, or in combination with usual care or other active treatments—improves LBP and is a cost-effective option. Three [26, 30, 40] of the four studies reported ICERs below the commonly cited threshold value of £20,000 per QALY, while the study by Herman *et al.* [35] found a multidisciplinary intervention that combines acupuncture with exercise and dietary advice, relaxation training and the provision of an educational booklet to be both less costly and more effective than standardised physiotherapy.

The clinical recommendations for effective management of back pain advise an individualised multi-modal package of care. A detailed bio-psychosocial assessment, including prognostic risk stratification, should inform targeted interventions. All patients will benefit from reassurance and advice and information on self-management. Further common interventions include physical activity and exercise programmes, manual therapy, with or without acupuncture, as part of a package of care empowering self-management but taking patient preference into account. Those with high risk stratification identifying barriers to recovery may benefit from more intensive intervention with a cognitive behavioural approach. While the clinical guidance for LBP is currently under review, the objective of this review is to assess cost-effectiveness, which does not imply clinical effectiveness.

4.2 Methodological issues and comparability

As mentioned above, various factors affect the quality of the identified studies and limit the extent to which reported results are comparable across, or even within, categories of interventions. Prominent amongst such factors are differences in the employed methods.

A first factor that may limit the comparability between studies is the form of economic analysis employed. The choice between CEA, CUA, or CBA depends upon influences such as the requirements of local decision-making bodies, the funding and organisation of local health care services and to some extent the expertise and judgement of the research team. Thus, the use of different forms of

analysis poses difficulties in making direct comparisons of the results between studies. However, even when the same form of analysis is adopted, there are many aspects of study design which could, and do, vary. For example, the results of any economic evaluation will differ if the primary measure of effect is changed [51, 52]. What has taken place in all of the studies reported, however, is a systematic comparison of alternative courses of action in terms of their costs and consequences. Hence, the headline findings of the different studies can be cautiously (with trends, patterns and contradictory findings highlighted) as a clear indication of the cost-effectiveness of the assessed interventions.

A further noteworthy issue relates to the adopted perspective. While good practice guidelines for conducting economic evaluations recommend adoption of a wide perspective which will reflect costs incurred to the health care system, patients, their family and their carers, and the economy as a whole, many of the identified studies adopted narrower perspectives. This is likely to have been a pragmatic choice, dictated by the nature of the health care system in place and by the interest of decision makers who are likely to use the reported results. For example, studies conducted in the USA, such as those by Haas *et al.* [24], Strong *et al.* [29] and Norton *et al.* [49] were carried out from the perspective of the organisation that bears the cost, typically the insurer. In contrast, studies which were conducted in countries with public health care coverage, such as those by Whitehurst *et al.* [45], Chuang *et al.* [44] and Aboagye *et al.* [48], typically adopt a health care system (NHS) and societal perspective.

Directly related to the chosen perspective is the inclusion of resource use and cost items in analyses. While good practice guidelines for conducting economic evaluations suggest that appraisal of interventions which are likely to affect absenteeism should include productivity costs [53, 54], there was considerable variation amongst studies in relation to the inclusion of such costs. The diversity in the resource use and costs included, as well as differences in sources of resource use and unit costs employed make comparisons of total costs between studies problematic. As private payments and productivity costs have been shown to constitute a significant share of the total cost of LBP [4, 55, 56], the inclusion or exclusion of such costs in the analysis is expected to have a sizeable impact on results. Similarly, if included, the impact of private healthcare costs can be more influential than payer costs. In general, a range of different interventions are associated with modest impact on QoL, such that additional intervention costs, if any, are not sufficiently large to prevent the interventions from being cost-effective compared to usual practice. However, differences in treatment costs and QALYs tend not to be statistically significant when interventions are compared to usual care. In this

context decision-makers need to be aware of how local service activity and costs are likely to compare to those represented in the published studies.

In relation to benefits, the identified studies employ a variety of health care measures to capture outcomes. These include a variety of condition and symptom specific measures about pain and disability, as well as QALYs. QALYs offer a generic measure of QoL that can facilitate comparisons, and this certainly has advantages over arguably narrower measures of outcome associated with CEAs. The multidimensional impact of LBP on people's usual activities suggests that, in the future, there is potential to use other QoL measures, such as wellbeing and capability measures [57], which offer an opportunity to compare QoL more holistically than the 'health' focus of QALYs.

Equally importantly, it must be noted that that evidence of cost-effectiveness does not necessarily imply clinical effectiveness [58]. Indeed there are many situations where intervention appear to result in clinical benefit, but economic analyses indicates that they are not cost-effective. Conversely, treatments which show little clinical benefit may result in cost savings that make them particularly appealing[58]. In addition, observing non-significant differences in QALYs (or costs) should not be interpreted as evidence of 'no effect', unless the study is specifically powered to detect such differences. Even if a study is suitably powered, it is widely agreed that, instead of focusing on hypothesis testing, conclusions about treatments' cost-effectiveness should not be drawn from interpreting the key measure of interest and the uncertainty around it [15]. Another factor which limits the accuracy of the reported aggregate value of health and economic outcomes, relates to the employed time horizon. The greatest share of studies were based on relatively short (typically 12 month) time horizons, which are likely to be inadequate in capturing the full extent of the long-term costs (or cost-savings) and benefits (or disbenefits) associated with treatments for LBP. Interestingly, in cases where a longer time horizon is adopted, this does affect the magnitude of the findings—and in the case of Niemisto *et al.* [25] it reversed the overall conclusion.

Comparisons were also hindered by the way final results were presented across studies. While the majority of studies calculated and presented incremental cost-effectiveness ratios, not all of them explicated the uncertainty around these estimates. The likelihood of assessed interventions to be cost-effective at different WTP values was typically presented in later studies. It is clear that journals do not necessarily require researchers to adhere to publication guidelines for economic evaluations.

All studies identified in this review were conducted in developed countries, mostly in North America, Western and Central Europe and Scandinavia. While, from a clinical perspective, populations in these countries can be expected to be similar and the effectiveness of treatments can be assumed to

be generalizable across countries, comparisons of cost-effectiveness results are likely to be unrealistic, given the considerable variability in the structure of health care systems, differences in the delivery and cost of health care services, and diversity in the bundle of services comprising usual care in different countries.

4.3 Strengths and limitations

The review poses particular strengths. In line with recommendations, we searched key electronic bibliographic databases and other sources, by constructing elaborate combinations of free text and indexing terms. Additional searches were carried out in reference lists of key known and identified references, including systematic reviews and official guidelines. Identified studies were independently assessed for inclusion against a set of predetermined criteria. No restrictions were applied on types of economic evaluation or analytic approach used: all types of full economic evaluations, as per the definition by Drummond *et al.* [15] were considered relevant, including both trial and model-based economic evaluation.

Nonetheless, our review presents specific limitations. In order to narrow the wide range of possible non-invasive and non-pharmacological interventions, we looked into those interventions for which there are indications that are safe and potentially beneficial in guidelines by NICE and APA/ASC. This, however, may have led to the exclusion of interventions which are not mentioned in these guidelines. In addition, given the evolving nature of the interventions, and in the light of changes in the methodology used to assess them, we limited the review to studies published in the last 15 years. This decision enabled us to reduce the chances of compromising comparability due to dissimilarities in the method of economic evaluations used, especially if such dissimilarities were introduced by studies assessing interventions which are now obsolete. While we have endeavoured to give authors' conclusions around cost-effectiveness of interventions, in cases where judgements were needed on what may be perceived to be cost-effective, we based such judgements on indicative values of WTP for an additional QALY suggested by NICE in the UK. However, it is likely that WTP values may vary across countries.

4.4 Comparison with other studies and future research

Given the diverse nature of the interventions (exacerbated by the complex combinations of elements making up a single intervention) and the differences in the aims and scope of the included studies, the scope for comparison between our review and other studies is limited. The study that is deemed to be closest to our review in terms of its aims and focus is that of Lin *et al.* [59][]. The authors [59] concluded that the cost-effectiveness of advice as an intervention for LBP is unclear, but

other interventions, including interdisciplinary rehabilitation, exercise, acupuncture, spinal manipulation and cognitive-behavioural therapy were, in general, cost-effective for people with sub-acute or chronic LBP. Findings in Lin *et al.* [59] and our review are in broad agreement. No studies evaluating the cost-effectiveness of medical yoga were identified or reported in the review by Lin *et al.* [59], though, in our review, we identified evidence which is supportive of yoga.

4.5 Conclusions

In summary, the reviewed evidence suggests that combined physical exercise and psychological treatments (CBT and risk stratification), provision of information, manual therapy (chiefly spinal manipulation and acupuncture) are cost-effective options for LBP. The identified evidence around physical exercise therapy is inconclusive; while medical yoga appears to be cost-effective compared to usual care, the finding for some active exercise programmes are equivocal.

Compliance with Ethical Standards

Disclosure of potential conflicts of interests

No funding has been received for this study.

Authors' conflicts of interest:

- LA: no conflict of interest declared
- PK: no conflict of interest declared
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- DW: no conflict of interest declared
- SD: no conflict of interest declared
- HM: no conflict of interest declared

Authors' contribution

- LA: Contributed to study conception and design, data collection, data analysis and interpretation, drafting the article, carrying out critical revisions.
- PK: Contributed to study conception and design, data collection, data analysis and interpretation, drafting sections of the article, carrying out critical revisions.
- SQ: Contributed to data collection, data analysis and interpretation, drafting sections the article, carrying out critical revisions.
- DW: Contributed to study conception and design, data collection, data analysis and interpretation, drafting sections of the article, carrying out critical revisions.
- SD: Contributed to data analysis and interpretation, carrying out critical revisions.
- HM: Contributed to study conception and design, data collection, data analysis and interpretation, drafting sections of the article, carrying out critical revisions.

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Tables

Table 1. Consensus on Health Economic Criteria (CHEC) checklist

Table 2. Characteristics of included studies

Table 1. Consensus on Health Economic Criteria (CHEC) checklist [16]

Study	Item																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Aboagye <i>et al.</i> [48]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Chuang <i>et al.</i> [44]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Critchley <i>et al.</i> [31]	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Foster <i>et al.</i> [47]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Haas <i>et al.</i> [24]	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N
Henchoz <i>et al.</i> [39]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	N	Y
Herman <i>et al.</i> [35]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N/A	Y	Y	Y	Y	Y
Hill <i>et al.</i> [43]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	Y	Y	Y	Y
Hollinghurst <i>et al.</i> [36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Jellema <i>et al.</i> [32]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Jensen <i>et al.</i> [46]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	N	N/A	N	Y	Y	Y	Y
Johnson <i>et al.</i> [33]	Y	Y	Y	Y	Y	N	N	N	N	Y	Y	Y	Y	N	N	N	Y	Y	Y
Kim <i>et al.</i> [40]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Lamb <i>et al.</i> [41]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y
Loisel <i>et al.</i> [18]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	N	Y	Y	Y	Y	Y
Molde Hagen <i>et al.</i> [20]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N	Y	Y	Y	Y
Niemisto <i>et al.</i> [21]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N/A	N	Y	Y	Y	Y
Niemisto <i>et al.</i> [25]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	N
Norton <i>et al.</i> [49]	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	N	Y	N

Ratcliffe <i>et al.</i> [26]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Rivero-Arias <i>et al.</i> [27]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	N
Rogerson <i>et al.</i> [42]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N/A	Y	Y	N	N	N
Schweikert <i>et al.</i> [28]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y
Skouen <i>et al.</i> [19].	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y	Y
Smeets <i>et al.</i> [38]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Strong <i>et al.</i> [29]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y	Y	Y
UK BEAM Trial team [22]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y
van der Roer <i>et al.</i> [37]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y
Whitehurst <i>et al.</i> [34]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	N
Whitehurst <i>et al.</i> [45]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Whitehurst <i>et al.</i> [50]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Williams <i>et al.</i> [23]	Y	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y
Witt <i>et al.</i> [30]	Y	Y	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	N/A	N	N	Y	Y	Y

Y: Yes; N: No; N/A: Not applicable.

Item 1: Is the study population clearly described? **Item 2:** Are competing alternatives clearly described? **Item 3:** Is a well-defined research question posed in answerable form? **Item 4:** Is the economic study design appropriate to the stated objective? **Item 5:** Is the chosen time horizon appropriate to include relevant costs and consequences? **Item 6:** Is the actual perspective chosen appropriate? **Item 7:** Are all important and relevant costs for each alternative identified? **Item 8:** Are all costs measured appropriately in physical units? **Item 9:** Are costs valued appropriately? **Item 10:** Are all important and relevant outcomes for each alternative identified? **Item 11:** Are all outcomes measured appropriately? **Item 12:** Are outcomes valued appropriately? **Item 13:** Is an incremental analysis of costs and outcomes of alternatives performed? **Item 14:** Are all future costs and outcomes discounted appropriately? **Item 15:** Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis? **Item 16:** Do the conclusions follow from the data reported? **Item 17:** Does the study discuss the generalizability of the results to other settings and patient/ client groups? **Item 18:** Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)? **Item 19:** Are ethical and distributional issues discussed appropriately?

Table 2. Characteristics of included studies

Study (year)	Intervention(s) and comparator(s)	Details of economic evaluation	Resource use, costs and outcomes
Combined physical exercise and psychological treatment			
Critchley <i>et al.</i> [31] (2007)	<p>Interventions:</p> <ul style="list-style-type: none"> - Spinal stabilisation physiotherapy - Physiotherapist-led pain management programme informed by a cognitive-behavioural approach <p>Comparator:</p> <p>Usual outpatient physiotherapy</p>	<p>Type of economic evaluation:</p> <p>CUA</p> <p>Analytic method employed:</p> <p>Trial-based economic evaluation</p> <p>Country:</p> <p>UK</p> <p>Time horizon:</p> <p>18 months</p> <p>Discounting:</p> <p>Yes (at 3.5% per year)</p> <p>Perspective:</p> <p>Health care system</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services <p>Measure of benefit used in economic evaluation (instrument used):</p> <p>QALY (EQ-5D)</p> <p>Main outcome of economic evaluation:</p> <p>Incremental cost per QALY gained: pain management programme was dominant (CEAC 65% at £30,000)</p>
Foster <i>et al.</i> [47] (2014) and Whitehurst <i>et al.</i> [50] (2015)	<p>Intervention:</p> <p>Stratified care based on a risk stratification tool</p> <p>Comparator:</p> <p>Usual care</p>	<p>Type of economic evaluation:</p> <p>CUA</p> <p>Analytic method employed:</p> <p>Economic evaluation based on a 'before-and-after' comparison of patient cohorts</p> <p>Time horizon:</p> <p>6 months</p> <p>Discounting:</p> <p>Not applicable</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services - Private - Productivity loss due to absence from paid employment. <p>Measure of benefit used in economic evaluation (instrument used):</p> <p>QALY (EQ-5D)</p> <p>Main outcome of economic evaluation:</p>

		Perspective: - Health care system - Societal	Incremental cost per QALY gained: Intervention was dominant (<i>CEAC reported at risk-group level only</i>)
Hill <i>et al.</i> [43] (2011) and Whitehurst <i>et al.</i> [45] (2012)	Intervention: Stratified care based on a risk stratification tool Comparator: Usual care	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: UK Time horizon: 12 months Discounting: Not applicable Perspective: Health care system Societal	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Productivity loss due to absence from paid employment. Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: Intervention was dominant (<i>CEAC 100% at £5,000</i>)
Johnson <i>et al.</i> [33] (2007)	Intervention: Physiotherapist-led group programme of exercise and education sessions using a cognitive behavioural therapy approach Comparator(s): General practitioner-led usual care plus receipt of an educational pack	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: UK Time horizon: 12 months Discounting: Not mentioned	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Private Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: £5,000 per QALY (<i>CEAC 90% at £30,000</i>)

		Perspective: Health care system	
Lamb <i>et al.</i> [41] (2010)	Intervention: Advice plus therapist-led assessment and 6 sessions of group cognitive behavioural intervention Comparator: Usual care plus advice	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: UK Time horizon: 12 months Discounting: Not applicable Perspective: Health care system	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: £1,786 per QALY (<i>CEAC 90% at £3,000</i>)
Norton <i>et al.</i> [49] (2015)	Intervention: Cognitive behavioural intervention from the Back Skills Training Trial reported by Lamb <i>et al.</i> [41] Comparator: Advice plus usual care from the Back Skills Training Trial reported by Lamb <i>et al.</i> [41]	Type of economic evaluation: CUA Analytic method employed: Economic evaluation based on a decision analytic model Country: USA Time horizon: 12 months and 120 months. Discounting: Yes (3% per year) Perspective:	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: \$7,197 per QALY over 12 months, \$5,855 per QALY over 120 months (<i>CEACs not reported</i>)

		Commercial payer	
Rogerson <i>et al.</i> [42] (2009)	<p>Intervention: Usual care plus multidisciplinary intervention consisting of 6 to 9 sessions of cognitive-behavioural and physical therapy</p> <p>Comparator: Usual care</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: USA</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Societal</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services. - Private payments - Income loss due to absence from paid employment. <p>Measure of benefit used in economic evaluation (instrument used): QALY (SF-6D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: intervention was dominant (<i>CEAC 91% at \$40,000</i>)</p>
Schweikert <i>et al.</i> [28] (2006)	<p>Intervention: Usual care plus psychologist-led 6 sessions of group cognitive behavioural therapy.</p> <p>Comparator: Usual care comprising 3-week intensive inpatient intervention at a specialist clinic</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Germany</p> <p>Time horizon: 6 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Societal</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services. - Private payments - Productivity loss due to absence from paid employment <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: intervention was dominant (<i>CEAC not reported</i>)</p>

Skouen <i>et al.</i> [19] (2002)	<p>Interventions: - Advice about exercise, lifestyle & fear avoidance; - Extensive 4-week programme of cognitive behavioural modification and coping strategies support and daily physical exercise.</p> <p>Comparator: Usual care</p>	<p>Type of economic evaluation: CBA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Norway</p> <p>Time horizon: 24 months</p> <p>Discounting: Yes (3.5% per year)</p> <p>Perspective: Societal</p>	<p>Main resource use items: - Intervention-related - Income loss due to absence from paid employment</p> <p>Measure of benefit used in economic evaluation: Return to paid work</p> <p>Main outcome of economic evaluation: Net benefit expressed in monetary terms: mean net productivity gain for advice intervention was US\$14,947 per male patient over two years. No gain for female patients was found.</p>
Whitehurst <i>et al.</i> [34] (2007)	<p>Intervention: Physiotherapist-led pain management programme targeting psychosocial factors</p> <p>Comparator: Physiotherapist-led 'best practice' physical therapy</p>	<p>Type of economic evaluation: - CUA - CEA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: UK</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Health care system</p>	<p>Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. - Private payments</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: £2,362 per QALY for physical therapy (CEAC 83% at £10,000)</p>

Physical exercise interventions			
Aboagye <i>et al.</i> [48] (2015)	Interventions: Medical yoga Exercise therapy Comparator: - Self-care advice	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: Sweden Time horizon: 12 months Discounting: Not applicable Perspective: - Employer - Societal	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Productivity loss due to absence from paid employment Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: medical yoga was dominant vs exercise; EUR 4,167 per QALY for medical yoga vs self-care advice. <i>(CEACs not reported)</i>
Chuang <i>et al.</i> [44] (2012)	Intervention: Yoga exercise plus usual care Comparator: Usual care	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: UK Time horizon: 12 months Discounting: Not applicable	Main resource use items: - Intervention-related costs - Primary care services - Secondary and specialist care services - Private - Productivity loss due to absence from paid employment Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained: £13,606 per QALY vs usual care <i>(CEAC</i>

		Perspective: - Health care system - Societal	72% at £20,000)
Henchoz <i>et al.</i> [39] (2010)	Intervention(s): Post-rehabilitation exercise programme Comparator(s): Post-rehabilitation usual care	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: Switzerland Time horizon: 12 months Discounting: Not applicable Perspective: Societal	Main resource use items: - Intervention-related costs - Primary care services - Secondary and specialist care services - Productivity loss due to absence from paid employment. Measure of benefit used in economic evaluation (instrument used): QALY (SF-6D) Main outcome of economic evaluation: Incremental cost per QALY gained: EUR 79,270 per QALY (<i>CEAC not reported</i>)
Rivero-Arias <i>et al.</i> [27] (2006)	Intervention(s): Physiotherapy treatment Comparator(s): Physiotherapist advice	Type of economic evaluation: CUA Analytic method employed: Trial-based economic evaluation Country: UK Time horizon: 12 months Discounting: Not applicable	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Private - Productivity loss due to absence from paid employment. Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D) Main outcome of economic evaluation: Incremental cost per QALY gained:

		Perspective: - Health care system - Societal	£3,010 per QALY (<i>CEAC 60% at £5,000 willingness to pay, not rising above 73% for higher thresholds</i>)
van der Roer et al. [37] (2008)	Intervention: Intensive group training Comparator: Usual care physiotherapy	Types of economic evaluations: -CEA -CUA Analytic method employed: Trial-based economic evaluation Country: Netherlands Time horizon: 12 months Discounting: Not applicable Perspective: Societal	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Private - Informal care-related - Productivity loss due to absence from paid and unpaid employment. Measure of benefit used in economic evaluation (instrument used): - LBP-related disability (RMDQ) - Pain intensity (11-point numerical rating scale) - General perceived effect (6-point ordinal scale) - QALYs (EQ-5D) instrument. Main outcomes of economic evaluation: - Cost per 1-point improvement on the RMDQ - Cost per 1-point improvement on the pain intensity scale - Cost per 1-point improvement on the general perceived effect scale - Incremental cost per QALY: EUR 5,141 per QALY (<i>CEAC not estimated</i>)
Smeets et al. [38] (2009)	Interventions: - Active physical treatment - Graded Activity plus problem solving training	Types of economic evaluation: - CEA - CUA	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services

	<ul style="list-style-type: none"> - Combined treatment (i.e. active physical treatment and graded activity plus problem solving training) 	<p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Netherlands</p> <p>Time horizon: 15.5 months (62 weeks)</p> <p>Discounting: No</p> <p>Perspective: Societal</p>	<ul style="list-style-type: none"> - Private (including over-the-counter medications, equipment and aids, travel expenses, informal care and paid housekeeping) - Productivity loss due to absence from paid employment. <p>Measure of benefit used in economic evaluation (instrument used):</p> <ul style="list-style-type: none"> - cost per reduction in LBP-related disability (RMDQ) - QALYs (EQ-5D) <p>Main outcome of economic evaluation:</p> <ul style="list-style-type: none"> - Incremental cost per 1-point improvement on the RMDQ - Incremental cost per QALY gained: graded activity plus problem solving training was dominant compared to combination treatment (<i>CEAC approximately 80% at EUR 20,000</i>)
Information and education intervention			
Loisel et al. [18] (2002)	<p>Interventions:</p> <ul style="list-style-type: none"> - Clinical rehabilitation (comprising clinical examination, participation in back school and, if necessary, a multidisciplinary work rehabilitation intervention) - Occupational intervention (comprising visits to occupational medicine physician and participatory ergonomics intervention) - Sherbrooke model (comprising a combination of clinical rehabilitation and occupational intervention) 	<p>Types of economic evaluation:</p> <ul style="list-style-type: none"> -CBA -CEA <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Canada</p> <p>Time horizon: 12 months and total follow up period for each</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services <p>Measure of benefit used in economic evaluation:</p> <ul style="list-style-type: none"> - Benefit (avoided absence from paid employment) measured in monetary units. - Number of fully compensated days because of back pain

	Comparator(s): Usual care	participant (mean of 77 months (6.4 years)) Discounting: Not mentioned Perspective: Payer (insurance provider)	Main outcome of economic evaluation: - Net benefit expressed in monetary units: all three interventions were associated with cost savings at 6.4 years compared to usual care. The largest mean saving was \$18,585 for the Sherbrooke model. - Cost per number of fully compensated days off work because of back pain: all three interventions were associated with a lower number of days on full benefits at 6.4 years compared to usual care. The smallest cost per saved day on full benefits was -\$88.40 for the occupational intervention.
Molde Hagen <i>et al.</i> [20] (2003)	Intervention: Spine clinic examination and provision of advice and information Comparator: Usual treatment in primary care	Type of economic evaluation: CBA Analytic method employed: Trial-based economic evaluation Country: Norway Time horizon: 36 months (3 years) Discounting: Yes (3.5% per year) Perspective: Societal	Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services - Productivity loss due to absence from paid employment. Measure of benefit used in economic evaluation (instrument used): Benefit due to avoided absence from paid employment measured in monetary units. Main outcome of economic evaluation: Net present value (i.e. difference between cost and benefit in monetary terms): mean net productivity gain for intervention was US\$2,822 per patient over three years.
Jensen <i>et al.</i> [46] (2013)	Intervention:	Type of economic evaluation:	Main resource use items:

	<p>Clinical examination, guidance and tailored 'return-to-work' programme.</p> <p>Comparator: Brief intervention involving clinical examinations by a rehabilitation doctor and a physiotherapist</p>	<p>-CEA -CBA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Denmark</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Health Care System Taxpayer Societal</p>	<p>- Intervention-related - Primary care services - Secondary and specialist care services. - Private (medicines) - Tax paid sick leave compensation</p> <p>Measure of benefit used in economic evaluation (instrument used): Employee sick leave averted</p> <p>Main outcome of economic evaluation: Incremental cost per 1 week averted sick leave</p>
Jellema <i>et al.</i> [32] (2007)	<p>Intervention: Minimal intervention strategy (identification and discussion of psychological prognostic factors)</p> <p>Comparator: Usual care</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Netherlands</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Societal</p>	<p>Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. - Private - Productivity loss due to absence from paid employment.</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: intervention was dominant for patients not at risk of losing their job. The ICER was EUR217 per week of sick leave</p>

			saved for patients who thought that they were at risk of losing their job. <i>(CEAC not reported)</i>
Strong et al. [29] (2006)	Interventions: <ul style="list-style-type: none"> - Self-management education led by a lay person; - Self-management education led by psychologist Comparator(s): Usual care plus a book on back pain care	Type of economic evaluation: CEA Analytic method employed: Trial-based economic evaluation Country: USA Time horizon: 12 months Discounting: Not applicable Perspective: Insurer (health care plan)	Main resource use items: <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services Measure of benefit used in economic evaluation: Number of low-impact back pain days Main outcome of economic evaluation: Incremental cost per additional low-impact back pain day: \$9.70 per low-impact back pain day for the lay intervention, and \$6.13 per low-impact back pain day for the psychologist intervention. <i>(CEACs not reported)</i>
Manual therapy interventions			
Haas et al. [24] (2005)	Intervention: Chiropractic care (spinal manipulation), exercise plan and self-care education Comparator: Usual medical care (including exercise plan and self-care education)	Type of economic evaluation: CEA Analytic method employed: Trial-based economic evaluation Country: USA Time horizon: 12 months Discounting:	Main resource use items: <ul style="list-style-type: none"> - Secondary and specialist care services (Medicare) Measure of benefit used in economic evaluation (instrument used): Pain, functional disability, patient satisfaction, physical health, mental health via a Visual Analogue Scale, the Revised Oswestry Disability Questionnaire and the Short Form 12 questionnaire.

		<p>Not applicable</p> <p>Perspective: Health provider (not explicitly stated)</p>	<p>Main outcome of economic evaluation: Additional cost per improvement in clinical outcomes: Chronic cohort: \$0.1 incremental total cost per unit of improvement in the pain measure at 12 months. Acute cohort: \$12 incremental total cost per unit of improvement in the pain measure at 12 months.</p>
Hollinghurst <i>et al.</i> [36] (2008)	<p>Intervention(s): - Therapeutic massage; - Therapeutic massage plus exercise prescription - Alexander technique (6 or 24 lessons); - Alexander technique (6 or 24 lessons) plus exercise prescription - Usual care plus exercise prescription</p> <p>Comparator(s): Usual care</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: UK</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: - Patient - Health care system - Societal</p>	<p>Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. - Private - Loss of earnings</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D).</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: £5,332 per QALY for Alexander technique (6 lessons) plus exercise prescription compared to normal care plus exercise (<i>CEAC 85% at £20,000</i>)</p>
Niemisto <i>et al.</i> [21, 25] (2003, 2005)	<p>Intervention(s): Physician consultation plus 4 sessions of combined manipulation and stabilisation exercises</p> <p>Comparator(s): Physician consultation alone plus an educational booklet</p>	<p>Type of economic evaluation: CEA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Finland</p>	<p>Main resource use items: - Primary care services - Secondary and specialist care services. - Private - Productivity loss due to absence from paid employment.</p> <p>Measure of benefit used in economic</p>

		<p>Time horizon: 12 months [21] and 24 months [25].</p> <p>Discounting: Not applicable</p> <p>Perspective: Societal</p>	<p>evaluation (instrument used): Pain (VAS), disability (Oswestry Low Back Pain Disability Questionnaire), mental depression (Finnish Depression Questionnaire), health related quality of life (15D), days on sick leave.</p> <p>Main outcome of economic evaluation: Additional cost per one- point change in pain score obtained from a visual analogue scale: a one-point increase in the intervention group compared to the control group in the VAS cost \$512 (<i>CEAC 75% at \$2,100 for a one-point increase in VAS</i>)</p>
UK BEAM Trial Team [22] (2004)	<p>Intervention(s): - 'Best care' plus exercise; - 'Best care' plus spinal manipulation; - 'Best care' plus spinal manipulation followed by exercise (combined treatment)</p> <p>Comparator(s): - 'Best care' in general practice</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: UK</p> <p>Time horizon: 12 months</p> <p>Discounting: Not applicable</p> <p>Perspective: - Health care system - Patient payments</p>	<p>Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. - Private</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D).</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: £8,700 for spinal manipulation relative to spinal manipulation followed by exercise (<i>CEAC 50% at £15,000</i>)</p>
Williams <i>et al.</i> [23] (2004)	<p>Intervention(s): Osteopathy clinic (3 or 4 sessions) plus</p>	<p>Type of economic evaluation: CUA</p>	<p>Main resource use items: - Intervention-related</p>

	<p>usual general practitioner care</p> <p>Comparator(s): Usual care (general practice)</p>	<p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: UK</p> <p>Time horizon: 6 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Health care provider</p>	<p>- Primary care services - Secondary and specialist care services.</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (EQ-5D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: £3,560 per QALY (<i>CEAC approximately 85% at £20,000</i>)</p>
Ratcliffe <i>et al.</i> [26] (2006)	<p>Intervention: Acupuncture treatment</p> <p>Comparator: Usual care</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: UK</p> <p>Time horizon: 24 months</p> <p>Discounting: Yes (at 3.5% per year)</p> <p>Perspective: Health care system Societal</p>	<p>Main resource use items: - Intervention-related - Primary care services - Secondary and specialist care services. - Private - Productivity loss due to absence from paid employment.</p> <p>Measure of benefit used in economic evaluation (instrument used): QALY (SF-6D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained</p>
Witt <i>et al.</i> [30] (2006)	<p>Intervention: Immediate access to acupuncture</p>	<p>Type of economic evaluation: CUA</p>	<p>Main resource use items: - Intervention-related costs</p>

	<p>Comparator: Acupuncture offered with a 3 month delay.</p>	<p>Analytic method employed: Economic evaluation based on randomised and nonrandomised studies</p> <p>Country: Germany</p> <p>Time horizon: 6 months</p> <p>Discounting: Not applicable</p> <p>Perspective: Societal</p>	<ul style="list-style-type: none"> - Use of primary care services - Use of secondary and specialist care services. - Private (out-of-pocket) payments <p>Measure of benefit used in economic evaluation (instrument used): QALY (SF-6D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: EUR 10,526 per QALY (<i>CEAC approximately 100% at EUR 30,000</i>)</p>
Herman <i>et al.</i> [35] (2008)	<p>Intervention: Neuropathic care, including acupuncture, relaxation exercises, exercise, dietary advice and a back care booklet.</p> <p>Comparator: Standardised physiotherapy education and a back care booklet</p>	<p>Type of economic evaluation: CUA</p> <p>Analytic method employed: Trial-based economic evaluation</p> <p>Country: Canada</p> <p>Time horizon: 6 months</p> <p>Discounting: Not applicable</p> <p>Perspective: - Employer - Participants - Society</p>	<p>Main resource use items:</p> <ul style="list-style-type: none"> - Intervention-related - Primary care services - Secondary and specialist care services. - Productivity loss due to absence from paid employment. <p>Measure of benefit used in economic evaluation (instrument used): QALY (SF-6D)</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: intervention was dominant (<i>CEAC not reported</i>)</p>
Kim <i>et al.</i> [40] (2010)	<p>Intervention:</p>	<p>Type of economic evaluation:</p>	<p>Main resource use items:</p>

	<p>Acupuncture in addition to usual care</p> <p>Comparator: Usual care</p>	<p>CUA</p> <p>Analytic method employed: Economic evaluation based on a decision analytic model</p> <p>Country: South Korea</p> <p>Time horizon: 72 months</p> <p>Discounting: Yes (5% per year)</p> <p>Perspective: Societal</p>	<ul style="list-style-type: none"> - Intervention-related costs - Primary care services - Secondary and specialist care services. - Private - Productivity loss due to absence from paid employment <p>Measure of benefit used in economic evaluation (instrument): QALY (estimated using SF-6D values from Witt <i>et al.</i> [30])</p> <p>Main outcome of economic evaluation: Incremental cost per QALY gained: KRW 3,421,394 (\$2,896) per QALY (CEAC 72% at KRW 20,000,000 (\$16,935))</p>
<p>QALY: quality-adjusted life year; CEA: cost-effectiveness analysis; CUA: cost-utility analysis; CBA: cost-benefit analysis; EQ-5D: EuroQol 5D (3-level) instrument; SF-6D: Short Form 6D instrument; RMDQ: Roland Morris disability questionnaire</p>			

Figure

Figure 1. PRISMA flow diagram depicting the process of record identification, screening and study inclusion

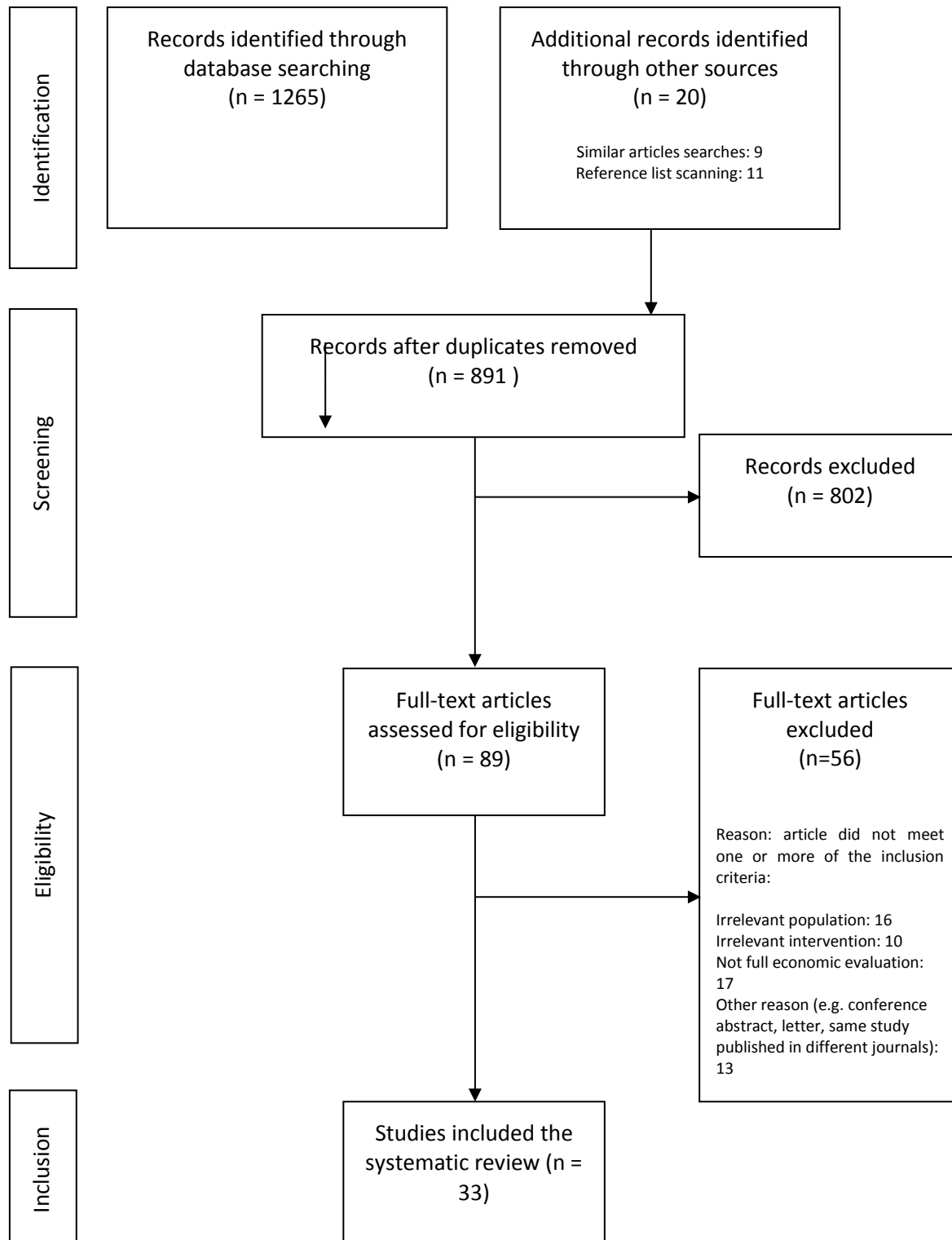


Figure 1. PRISMA flow diagram depicting the process of record identification, screening and study inclusion

Appendices and online materials

Online Resource 1: Table 1. Categorisation of interventions

Online Resource 1: Search strategy used in MEDLINE

Online Resource 1: Table 2. Inclusion and exclusion criteria

Online Resource 1.

Table 1. List of non-invasive and non-pharmacological interventions.

Intervention category	Examples of relevant treatments
Combined physical exercise and psychological	Cognitive behavioural therapy ^c Interdisciplinary rehabilitation ^b
Physical exercise therapy	Aerobic activity ^c Movement instruction ^a Muscle strengthening ^c Postural control ^a Stretching ^c Yoga ^b Superficial heat ^b Progressive relaxation ^b Functional restoration ^b
Manual therapy	Spinal manipulation ^c Spinal mobilisation ^a Massage ^c Acupuncture ^c
Information and education	Advice & information on self-management ^a
^a Included in NICE guideline [13] only; ^b Included in APS/ASC guideline [10] only; ^c Included in both NICE and APS/ASC guidelines	

Online Resource 1.

Search strategy used in MEDLINE

1. low back pain/ or low back pain.ti,ab.
2. lumbago/ or lumbago.ti,ab.
3. backache/ or backache.ti,ab.
4. dorsalgia/ or dorsalgia.ti,ab.
5. lower back pain/ or lower back pain.ti,ab.
6. lumbar pain/ or lumbar pain.ti,ab.
7. back pain/ or back pain.ti,ab.
8. spin* disease*/ or spin* disease*.ti,ab.
9. coccydynia/ or coccydynia.ti,ab.
10. spinal pain/ or spinal pain.ti,ab.
11. dorsopathy/ or dorsopathy.ti,ab.
12. lumbar disease*/ or lumbar disease*.ti,ab.
13. back disorder*/ or back disorder*.ti,ab.

14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15. health econom*.ti,ab.
16. economic* evaluation*.ti,ab.
17. economic* analys#s.ti,ab.
18. cost effect*.ti,ab.
19. cost-effect*.ti,ab.
20. cost benefit*.ti,ab.
21. cost-benefit*.ti,ab.
22. cost utilit*.ti,ab.
23. cost-utilit*.ti,ab.
24. cost consequence* analys#s.ti,ab.
25. cost-consequence* analys#s.ti,ab.
26. cost minimi#ation analys#s.ti,ab.
27. cost-minimi#ation analys#s.ti,ab.
28. economic* aspect*.ti,ab.
29. health care cost*.ti,ab.
30. cost analys#s.ti,ab.

31. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30

32. advice.ti,ab.
33. information.ti,ab.
34. educat*.ti,ab.
35. physical activit*.ti,ab.
36. exercise*.ti,ab.
37. aerobic exercise*.ti,ab.
38. aerobic activit*.ti,ab.
39. movement* instruction*.ti,ab.
40. muscle strengthen*.ti,ab.
41. postural control.ti,ab.
42. stretching.ti,ab.
43. manual therap*.ti,ab.
44. spinal manipulation*.ti,ab.
45. spinal mobili#ation*.ti,ab.
46. massage.ti,ab.
47. acupuncture.ti,ab.
48. psychotherap*.ti,ab.

49. psychological therap*.ti,ab.
 50. psychological treatment*.ti,ab.
 51. psychological intervention*.ti,ab.
 52. cognitive therap*.ti,ab.
 53. cognitive treatment*.ti,ab.
 54. cognitive intervention*.ti,ab.
 55. behaviour therap*.ti,ab.
 56. behaviour treatment*.ti,ab.
 57. behaviour intervention*.ti,ab.
 58. behavior therap*.ti,ab.
 59. behavior treatment*.ti,ab.
 60. behavior intervention*.ti,ab.
 61. cognitive behavior*.ti,ab.
 62. cognitive behaviour*.ti,ab.
 63. cognitive behavioral therap*.ti,ab.
 64. cognitive behavioural therap*.ti,ab.
 65. CBT.ti,ab.
 66. progressive relaxation*.ti,ab.
 67. interdisciplinary rehabilitation.ti,ab.
 68. functional restoration*.ti,ab.
 69. superficial heat.ti,ab.

70. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69

71. 14 and 31 and 70

72. limit 71 to English

73. limit 72 to yr="2000 -Current"

Online Resource 1.

Table 2. Inclusion and exclusion criteria

Aspect	Inclusion criteria
Population	Human subjects with non-specific acute, sub-acute or chronic low back pain.
Intervention	Non-pharmacological interventions specified in the National Institute for Health and Care Excellence guideline [56] for early management of low back pain and in the American Pain Society/American College of Physicians clinical guidelines [10].
Comparator(s)	Any comparators, including: <ul style="list-style-type: none">• 'do nothing'/placebo/sham interventions• pharmacological interventions• surgery, and/or• other non-pharmacological interventions
Outcomes	Cost per-unit of effect (e.g., natural unit, quality-adjusted life year), presented as either a summary measure or in a disaggregated form.
Study design	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, cost-consequences analysis or cost-minimisation analysis.
Other restrictions	Published between January 2000 to July 2015. Published in English